Fig. 1: Comparison of porcine to human FVIII protein sequence (numbers refer to mature human FVIII; in the porcine sequence, only discrepant aminoacids are displayed; identical aminoacids are indicated by a ".")

```
241  . . . . . K . . . . . .  Porcine FVIII
240  R S L P G L I G C H R K S V Y W H V I G  Human FVIII

261  . . . S . . . . . . . . . . . . . . .  Porcine FVIII
260  M G T T P E V H S I F L E G H T F L V R  Human FVIII

281  H . . . . . L . . . . . F  Porcine FVIII
280  N H R Q A S L E I S P I T F L T A Q T L  Human FVIII

301  . . . . . H . G .  Porcine FVIII
300  L M D L G Q F L L F C H I S S H Q H D G  Human FVIII

321  . . . H . R . E . . A . . . . . R . A  Porcine FVIII
320  M E A Y V K V D S C P E E P Q L R M K N  Human FVIII

341  D . . - . . . . . N . Y . . D . . . . .  Porcine FVIII
340  N E E A E D Y D D D L T D S E M D V V R  Human FVIII

360  L . G . D V S P . . . . . .  Porcine FVIII
360  F D D D N S P S F I Q I R S V A K K H P  Human FVIII

380  . . . . . S . . . . . A .  Porcine FVIII
380  K T W V H Y I A A E E E D W D Y A P L V  Human FVIII

400  P S . S . . . . . L . . . S . . . . .  Porcine FVIII
400  L A P D D R S Y K S Q Y L N N G P Q R I  Human FVIII

420  . . . . . A . . V . . . . V . . . . .  Porcine FVIII
420  G R K Y K K V R F M A Y T D E T F K T R  Human FVIII

440  K . . P Y . . . . . .  Porcine FVIII
440  E A I Q H E S G I L G P L L Y G E V G D  Human FVIII

460  . . . . . K . . . . . .  Porcine FVIII
460  T L L I I F K N Q A S R P Y N I Y P H G  Human FVIII

480  . . . . S A . H P G . . L . . W . . . .  Porcine FVIII
480  I T D V R P L Y S R R L P K G V K H L K  Human FVIII

500  . M . . . . . T . . . . . .  Porcine FVIII
500  D F P I L P G E I F K Y K W T V T V E D  Human FVIII

520  . . . . . S I . L  Porcine FVIII
520  G P T K S D P R C L T R Y Y S S F V N M  Human FVIII

540  . K . . . . . .  Porcine FVIII
540  E R D L A S G L I G P L L I C Y K E S V  Human FVIII

560  . . . . . M . . . . . .  Porcine FVIII
560  D Q R G N Q I M S D K R N V I L F S V F  Human FVIII

580  . . . Q . . . . A . . . . . D  Porcine FVIII
580  D E N R S W Y L T E N I Q R F L P N P A  Human FVIII

600  . L . P Q . . . . . .  Porcine FVIII
600  G V Q L E D P E F Q A S N I M H S I N G  Human FVIII
```

Fig. 2: **Mutations of human FVIII which are based on a protein comparison with porcine FVIII (does not comprise all mutations which are possible according to the invention):**

aa (mature human FVIII)	Amino acid in human sequence	Mutated to	Or mutated to
318	D	G	K
337	M	R	
340	N	D	
349	D	N	K
364	N	D	
403	D	S	K
434	E	V	K
440	E	K	
468	Q	K	
484	R	S	E
489	R	G	E
583	R	Q	E
599	A	D	
604	E	Q	K

Fig. 3: Mutations of human FVIII which are based on an analysis of existing human mutations leading to an enhanced dissociation of the A2 domain (does not comprise all mutations possible according to the invention)

aa (Mature human FVIII)	From (human sequence)	To	Comments
284	A	K	A to E leads to enhanced dissociation of A2 domain
1948	G	K	G to D leads to enhanced dissociation of A2 domain